Baseline Predictors of Renal Failure in Transcatheter Aortic Valve Implantation

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Abstract: BACKGROUND Acute kidney injury (AKI) post transcatheter aortic valve implantation (TAVI) is associated with worsened short- and long-term outcomes. We sought to identify significant baseline predictors of AKI and establish a high-risk group within patients enrolled in the multicenter SWISS-TAVI cohort. METHODS AND RESULTS A total of 526 patients who underwent TAVI were included in our analysis. Patients on hemodialysis were excluded. Within the first week after valve implantation, fifty patients (9.5%) developed AKI. There was a significantly higher prevalence of diabetes mellitus in the AKI group (45% vs 28%; P=.02). The odds ratio (OR) for patients suffering from diabetes mellitus who developed AKI was 1.9 after multivariable binary regression analysis (95% confidence interval, 1.018-3.553; P=.04). Chronic kidney disease (CKD) stage 4 was more prevalent in the AKI group (26% vs 14%; P=.04). Every 1 mg/dL creatinine above normal level at baseline increased AKI risk by a factor of 1.6 (OR, 1.605; 95% CI, 1.111-2.319; P=.01). Age, gender, body mass index, history of dyslipidemia, and history of hypertension were similar between the groups. In the diabetic population of 155 patients (29.5%), AKI developed in 22 patients (14.2%), compared with the non-diabetic population of 370 patients (70.5%), where AKI developed in 27 patients (7.3%). In the diabetic population, an elevation by 1 mg/dL in baseline creatinine was an independent predictor of developing kidney injury (OR, 2.061; 95% CI, 1.154-3.683; P=.02, while in non-diabetic patients, neither baseline glomerular filtration rate, CKD grade, STS score, EuroScore II, ACEF score, nor procedural contrast usage were predictors of AKI. CONCLUSION Diabetics with CKD stage 4 (as defined by the Kidney Disease: Improving Global Outcomes criteria) constitute a high-risk group for developing AKI after TAVI. In this high-risk subgroup, baseline creatinine in combination with amount of contrast agent used were strong risk factors for developing AKI. AKI in non-diabetics was less predictable by baseline characteristics.

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ABSTRACT: Background. Acute kidney injury (AKI) post transcatheter aortic valve implantation (TAVI) is associated with worsened short- and long-term outcomes. We sought to identify significant baseline predictors of AKI and establish a high-risk group within patients enrolled in the multicenter SWISS-TAVI cohort. **Methods and Results.** A total of 526 patients who underwent TAVI were included in our analysis. Patients on hemodialysis were excluded. Within the first week after valve implantation, fifty patients (9.5%) developed AKI. There was a significantly higher prevalence of diabetes mellitus in the AKI group (45% vs 28%; *P*=.02). The odds ratio (OR) for patients suffering from diabetes mellitus who developed AKI was 1.9 after multivariable binary regression analysis (95% confidence interval, 1.018-3.553; *P*=.04). Chronic kidney disease (CKD) stage ≥4 was more prevalent in the AKI group (26% vs 14%; *P*=.04). Every 1 mg/dL creatinine above normal level at baseline increased AKI risk by a factor of 1.6 (OR, 1.605; 95% CI, 1.111-2.319; *P*=.01). Age, gender, body mass index, history of dyslipidemia, and history of hypertension were similar between the groups. In the diabetic population of 155 patients (29.5%), AKI developed in 22 patients (14.2%), compared with the non-diabetic population of 370 patients (70.5%), where AKI developed in 27 patients (7.3%). In the diabetic population, an elevation by 1 mg/dL in baseline creatinine was an independent predictor of developing kidney injury (OR, 2.061; 95% CI, 1.154-3.683; *P*=.02, while in non-diabetic patients, neither baseline glomerular filtration rate, CKD grade, STS score, EuroScore II, ACEF score, nor procedural contrast usage were predictors of AKI. **Conclusion.** Diabetics with CKD stage ≥4 (as defined by the Kidney Disease: Improving Global Outcomes criteria) constitute a high-risk group for developing AKI after TAVI. In this high-risk subgroup, baseline creatinine in combination with amount of contrast agent used were strong risk factors for developing AKI. AKI in non-diabetics was less predictable by baseline characteristics.

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KEY WORDS: acute kidney injury, Swiss TAVI cohort, TAVI

Acute kidney injury (AKI) is a known complication after transcatheter aortic valve implantation (TAVI),[1-7] with a reported incidence of 8.3%-57.0%.[1,5] Severe AKI is one of the strongest predictors of postprocedural 30-day mortality and is associated with worse mid- and long-term outcomes.[3,4,8-10] Discrepancies still exist regarding the association between AKI and mortality.[11,12] Helgason et al[12] found AKI to be an independent predictor of procedural mortality (odds ratio [OR], 5.89; 95% confidence interval [CI], 1.99-18.91), but not of long-term survival (hazard ratio [HR], 1.44; 95% CI, 0.86-2.42).

On the other hand, chronic kidney disease (CKD) was associated with worse outcomes.[13-16] Uncertainty exists with regard to predictors of AKI; different baseline characteristics and procedural circumstances were suggested as predictors, including commonly used surgical risk scores, such as the EuroScore II and Society of Thoracic Surgeons (STS) score. However, the currently available scores lack predictive accuracy.[17-19]

In the current study, we sought to assess significant predictors of AKI in patients undergoing TAVI, solely by identifying the strongest baseline risk factors.

Methods

Patients. All patients included in the current study were enrolled in the SWISS TAVI registry, which mandated obtaining a voluntary consent prior to any intervention.

The Zurich study population included 335 consecutive patients who underwent TAVI at the University Hospital of Zurich from 2012 to 2015 and had completed 1-year follow-up. A group of 191 consecutive TAVI patients from Cardiocentro Ticino were also included in the current analysis, bringing the entire study population to 526 patients who were evaluated for the development of postprocedural AKI within 7 days post TAVI. All patients were assessed for perioperative and long-term risk for TAVI by means of EuroScore II; STS score; baseline age, creatinine and ejection fraction (ACEF) score; echocardiography; clinical presentation; and baseline characteristics, such as laboratory parameters and comorbidities.

Definitions. *Baseline CKD stages* were defined according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria, along with the definition and staging of AKI. *AKI* was defined as any of the following: increase in serum creatinine by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; increase in

serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or urine volume <0.5 mL/kg/h for 6 hours. The recommendations of the KDIGO of the United States National Kidney Foundation were taken under consideration.[20,21]

TAVI and main access site. Indication for TAVI was discussed within an interdisciplinary heart team. Access site was femoral in 474 patients (90.0%), transapical in 32 patients (6.0%), subclavian in 15 patients (2.9%), and direct aortic in 5 patients (1.0%). The valve was selected by the operators; the most commonly implanted valves were the CoreValve (Medtronic) in 237 patients (45.0%) and Edwards valves (Edwards Lifesciences) in 216 patients (41.0%).

Statistical analysis. Continuous variables are expressed as median with interquartile range (IQR) and were compared between patients with and without AKI by means of Mann-Whitney U-tests (all non-normally distributed by looking at the data and verifying with Shapiro-Wilk's test). Categorical data are expressed as percentiles within the AKI and non-AKI groups, and were compared using the Fisher's exact test. For our analysis, we further divided patients into diabetics and non-diabetics. Variables with a probability value of $P<.05$ in the univariable analysis, as well as other factors with clinical reasoning, were included in a multivariate logistic regression model, with AKI as the dependent variable. The final model was assessed for calibration by means of the Hosmer-Lemeshow goodness-of-fit test.

All probability values and confidence intervals were two-sided. The level of statistical significance was set at a probability value of $P<.05$. Statistical analysis was performed using SPSS Statistics software, version 24.0 (IBM).

Results

Analysis of the whole population. Baseline characteristics included a high prevalence of arterial hypertension in 395 patients (75.0%) and diabetes mellitus (DM) in 155 patients (29.5%), with 334 patients (63.5%) classified as either New York Heart Association III or IV. Median overall STS score was 4.87% (range, 0.7%-37.6%; mean, 6.60%). A complete list of baseline characteristics is shown in Table 1.

A total of 50 patients (9.5%) developed postprocedural AKI within the first 7 days (Figure 1). Patients who developed AKI were more likely to have DM (44.9% vs 27.9%; $P=.02$), CKD grade ≥IV (26% vs 13.9%; $P=.04$), and higher baseline creatinine (1.30 mg/dL [IQR, 0.98-1.75 mg/dL] vs 1.09 mg/dL [IQR, 0.88-1.36 mg/dL]; $P=.01$). On the other hand, there were no significant differences in echocardiographic findings between the groups at baseline. The complete list of baseline characteristics and risk factors after TAVI can be found in Table 2.

Of the multiple risk scores assessed at baseline, only STS was significantly higher in those who developed AKI (6.45% [IQR, 3.48%-10.01%] vs 4.84% [IQR, 3.07%-7.60%]; $P=.03$) (Table 2).

For the assessment of possible predictive factors in the development of AKI, we applied a univariate logistic regression model (Figure 3). On a multivariate logistic regression model (corrected for baseline creatinine, DM, STS score, and coronary revascularization), baseline creatinine (OR, 1.605; 95% CI, 1.111-2.319; $P=.01$) and DM (OR, 1.902; 95% CI, 1.018-3.553; $P=.04$) were the only significant predictors of postprocedural AKI. The model was well calibrated by means of Hosmer-Lemeshow test ($Chi^2=4.389$; $P=.82$).

Subanalysis of AKI in DM patients. We compared baseline characteristics and risk factors of the diabetes subgroup with regard to AKI after TAVI (Table 3). Diabetic patients comprised 155 patients (29.5% of the study population), of which 22 (14.2%) developed AKI. Baseline ACEF score was significantly higher among diabetic AKI patients (4.36 [IQR, 3.57-5.81] vs 3.32 [IQR, 1.46-4.79]; $P<.01$) (Supplementary Figure S1) translating into a lower baseline GFR (35.50 mL/min/1.73 m^2 [IQR, 27.62-45.13 mL/min/1.73 m^2] vs 45.41 mL/min/1.73 m^2 [IQR 34.19-66.18 mL/min/1.73 m^2]; $P<.01$) as well as a higher incidence of CKD grade ≥IV (40.9% vs 12.9%; $P<.01$). The overall amount of contrast used in diabetics who developed AKI was lower (84.00 mL [IQR, 55.00-295.75 mL] vs 140.00 mL [IQR, 72.60-270.00 mL]); however, a higher ratio of contrast to GFR was documented in this group (mean, 5.72 vs 4.32; median, 2.96 [IQR, 1.48-5.86] vs 2.14 [IQR, 1.20-6.56]) (Supplementary Figure S2). Baseline echocardiographic assessment was not different among the groups.

In the diabetic subgroup, a univariate logistic regression model for the assessment of possible predictive factors in the development of AKI is shown in Figure 4. For the multivariate logistics regression model, we corrected for contrast agent (mL)/GFR (OR, 0.982; 95% CI, 0.893-1.080; $P=.71$) and baseline creatinine (OR, 2.061; 95% CI, 1.154-3.683; $P=.02$). This model was also considered well calibrated by means of Hosmer-Lemeshow test ($Chi^2=4.607$; $P=.80$). In the diabetic population, an elevation by 1 mg/dL in baseline creatinine was associated with a twofold increased risk of developing AKI (OR, 2.061; 95% CI, 1.154-3.683).

The univariate and multivariate analyses within the non-DM group did not yield any significant predictors of AKI. No kidney function assessment had any significance in foreseeing AKI. However, lower hemoglobin levels had a significant correlation in its development after TAVI (112.00 g/L [IQR, 96.50-136.00 g/L]) vs 125.00 g/L [IQR, 114.50-136.00 g/L]; $P=.04$).

Discussion

AKI is one of the most commonly occurring adverse events in TAVI and is associated with lower survival[5,22,23] post TAVI. In our analysis, which comprised mainly intermediate surgical risk patients with a median STS of 4.87% (mean, 6.60%; 95% CI, 6.12-7.08), we found that AKI occurred in 9.5% of patients, of which 78.8% had stage 1 AKI, 18.2% had stage 2 AKI, and 3.0% had stage 3 AKI. DM plays an

Table 1. Baseline characteristics of the entire study population.

	n = 526
Diabetes mellitus	155 (29.5%)
Peripheral artery disease	90 (17.1%)
Body mass index (kg/m²)	range, 15.4-44.4; mean, 26.6
Dyslipidemia	242 (46.0%)
Arterial hypertension	395 (75.1)
Coronary artery disease	273 (51.9%)
History of cerebrovascular accident	53 (10.1%)
History of myocardial infarction	71 (13.5%)
Previous pacemaker implantation	53 (10.1%)
History of PCI	135 (25.7%)
Chronic obstructive pulmonary disease	86 (16.4%)
New York Heart Association class III or IV	334 (63.5%)
Coronary artery bypass grafting	82 (15.6%)
Previous aortic valvuloplasty	8 (1.5%)
Chronic kidney disease grade IV or V	79 (15.0%)
Male sex	272 (51.7%)
Concomitant procedure	61 (11.6%)
Coronary revascularization	29 (5.5%)
Other concomitant procedure	35 (6.7%)
Severe pulmonary artery hypertension	60 (11.4%)
Aspirin	365 (69.4%)
Clopidogrel	201 (38.2%)
Vitamin K antagonist	130 (24.7%)
Novel anticoagulants	21 (4.0%)
VKA or novel anticoagulants	151 (28.7%)
Brain natriuretic peptide (pg/mL) [n = 473]	median, 1266; range, 11.0-34070; mean, 2723
Baseline ACEF score [n = 519]	median, 3.36; range, 0.66-8.99; mean, 3.47
Age (years)	range, 36.9-96.6; mean, 81.9
GFR (mL/min/1.73 m²) [n = 524]	range, 9.4-354.8; mean, 50.9
Creatinine baseline (mg/dL) [n = 525]	range, 0.16-6.20; mean, 1.24
EuroScore II (%) [n = 477]	median, 3.67; range, 0.60-42.58; mean, 5.3
STS score (%) [n = 525]	median, 4.87; range, 0.70-37.60; mean, 6.6
Hemoglobin (g/L) [n = 335]	range, 66-159; mean, 120
Total constrast during TAVI (mL) [n = 519]	range, 4.00-960; mean, 189
Contrast/GFR ratio [n = 517]	range, 0.15-35.98; mean, 4.46
Echocardiographic characteristics	
Aortic valve area (cm²) [n = 484]	range, 0.25-1.60; mean, 0.73
Mitral regurgitation ≥ grade 2	90 (17.1%)
Tricuspid regurgitation ≥ grade 2	48 (9.1%)
Ejection fraction (%) [n = 521]	range, 17.0-88.0; mean, 53.7
Mean gradient (mm Hg) [n = 515]	range, 5.0-98.0; mean, 44.6

Data available for entire study population [n = 526], unless otherwise noted within brackets.
ACEF = age, creatinine, ejection fraction; GFR = glomerular filtration rate by Cockcroft-Gault equation; VKA = vitamin K antagonist.

important role in predicting AKI post TAVI (OR, 1.9; 95% CI, 1.018-3.553; *P*=.04) along with CKD stage IV and V, creatinine at baseline, and STS risk score for mortality. This result is in line with previous reports[11,24,25] that showed an OR of 6.722 (*P*<.01) or a HR of 1.6 (95% CI, 1.1-2.4) in DM patients.[11,25] Diabetics are at a higher risk for any operation or invasive treatment and consequently have a lower survival advantage.[26,27] Patients who developed AKI (9.5%) had significantly higher baseline creatinine (1.30 mg/dL vs 1.09 mg/dL; *P*=.01) and other risk factors, while other commonly known risk factors like arterial hypertension (*P*=.49) and peripheral artery disease (*P*=.17) did not statistically differ between the groups. In other published studies, hypertension, chronic obstructive pulmonary disease, and blood transfusion were found to also be predictive factors.[23] This difference could be explained by our intermediate-risk population; in addition, most of the factors we assessed are preprocedural baseline characteristics. None of the echocardiographic findings were predictors of AKI.

To further substantiate our findings, we studied the influence of contrast volume, which is correlated with the development of contrast-induced nephropathy after TAVI.[28,29] When comparing the mean total amount of 110.0 mL contrast used in patients who developed AKI from our cohort to other studies as listed in the meta-analysis by Wang et al,[30] the volume was on the lower end but could be further reduced in the future. There, the median volume of contrast agent applied to the whole study population ranged from 79 ± 55 mL to 242 ± 101 mL. Patients who developed AKI post TAVI received

Table 2. Baseline and echocardiographic characteristics for entire population stratified by presence of AKI post TAVI.

Characteristics	Total Patients (n)	No AKI (n = 476; 90.5%)	AKI (n = 50; 9.5%)	*P*-Value
Diabetes mellitus	155	133 (27.9%)	22 (44.9%)	.02
Peripheral artery disease	90	78 (16.4%)	12 (24.0%)	.17
Body mass index (kg/m²)	526	26.05 (23.43-29.30)	27.20 (24.33-30.68)	.11
Dyslipidemia	242	219 (46.0%)	23 (46.0%)	>.99
Arterial hypertension	395	355 (74.6%)	40 (80%)	.49
Coronary artery disease	273	247 (51.9%)	26 (52.0%)	>.99
History of cerebrovascular accident	53	45 (9.5%)	8 (16%)	.14
History of myocardial infarction	71	67 (14.1%)	4 (8.0%)	.28
Previous pacemaker implantation	53	46 (9.7%)	7 (14%)	.32
History of percutaneous coronary intervention	135	123 (25.8%)	12 (24.0%)	.87
Chronic obstructive pulmonary disease	86	78 (16.4%)	8 (16%)	>.99
New York Heart Association III or IV	334	299 (62.8%)	35 (70%)	.36
Coronary artery bypass graft	82	75 (21.3%)	7 (20.6%)	>.99
Previous aortic valvuloplasty	8	8 (1.7%)	0 (0.0%)	>.99
Chronic kidney disease grade IV or V	79	66 (13.9%)	13 (26%)	.04
Male sex	272	242 (50.8%)	30 (60%)	.24
Concomitant procedure	61	54 (11.3%)	7 (14.3%)	.49
Coronary revascularization	29	24 (5.0%)	5 (10.2%)	.18
Other concomitant procedure	35	32 (6.7%)	3 (6.1%)	>.99
Severe pulmonary artery hypertension	60	54 (12%)	6 (13.6%)	.81
Aspirin	365	333 (70.9%)	32 (66.7%)	.62
Clopidogrel	201	186 (39.6%)	15 (31.3%)	.28
Vitamin K antagonist	130	119 (25.3%)	11 (22.9%)	.86
Novel anticoagulants	21	20 (5.4%)	1 (2.8%)	>.99
Vitamin K antagonist or novel anticoagulants	151	139 (29.6%)	12 (25.0%)	.62
Brain natriuretic peptide (pg/mL)	473	1166 (361-3028.)	1692 (698-3275)	.22
Baseline ACEF score (%)	519	3.36 (2.07-4.62)	3.86 (1.91-4.94)	.32
Age (years)	526	82.90 (78.93-86.73)	82.38 (79.30-85.15)	.63
Weight (kg)	525	71.00 (62.00-81.00)	76.50 (65.75-84.25)	.06
GFR (mL/min/1.73 m²)	524	47.86 (35.82-63.72)	41.23 (28.76-63.65)	.20
Creatinine baseline (mg/dL)	525	1.09 (0.88-1.36)	1.30 (0.98-1.75)	.01
EuroScore II (%)	477	3.58 (2.00-6.33)	4.76 (2.53-7.46)	.10
STS score (%)	525	4.84 (3.07-7.60)	6.45 (3.48-10.01)	.03
Hemoglobin (g/L)	335	122.00 (111.00-133.50)	111.50 (98.50-133.75)	.04
Total constrast volume during TAVI (mL)	519	138.50 (78.75-280.00)	110.00 (60.00-300.00)	.52
Contrast/GFR ratio	517	2.97 (1.55-5.89)	2.40 (1.38-7.33)	.69
Echocardiographic characteristics				
Aortic valve area (cm²)	484	0.70 (0.60-0.90)	0.75 (0.60-0.90)	.50
Mitral regurgitation ≥ grade II	90	77 (16.6%)	13 (27.1%)	.08
Tricuspid regurgitation ≥ grade II	48	45 (10%)	3 (6.4%)	.46
Ejection fraction (%)	521	58.00 (45.00-61.75)	56.00 (45.00-62.00)	.86
Mean gradient (mm Hg)	515	43.00 (34.00-55.00)	40.00 (33.00-52.50)	.30

Data provided as number (%) or median (range). AKI = acute kidney injury; GFR = glomerular filtration rate by Cockcroft-Gault equation.

Table 3. Baseline and echocardiographic characteristics for diabetic subgroup stratified by presence of AKI post TAVI.

Characteristics	Total Patients (n)	No AKI (n = 133; 85.8%)	AKI (n = 22; 14.2%)	*P*-Value
Dyslipidemia	87	74 (55.6%)	13 (59.1%)	.82
Arterial hypertension	125	105 (78.9%)	20 (90.9%)	.25
Coronary artery disease	90	79 (59.4%)	11 (50.0%)	.49
History of cerebrovascular event	17	14 (10.5%)	3 (13.6%)	.71
Peripheral artery disease	35	30 (22.6%)	5 (22.7%)	>.99
History of myocardial infarction	34	32 (24.1%)	2 (9.1%)	.16
Previous pacemaker implantation	18	14 (10.6%)	4 (18.2%)	.29
History of percutaneous coronary intervention	52	46 (34.6%)	6 (27.3%)	.63
Chronic obstructive pulmonary disease	26	23 (17.3%)	3 (13.6%)	>.99
Dyspnea New York Heart Association III or IV	109	93 (69.9%)	16 (72.7%)	>.99
Coronary artery bypass graft	31	27 (24.8%)	4 (30.8%)	.74
Previous aortic valvuloplasty	2	2 (1.5%)	0 (0.0%)	>.99
Chronic kidney disease grade IV or V	26	17 (12.9%)	9 (40.9%)	<.01
Male sex	91	79 (59.4%)	12 (54.5%)	.82
Female sex	64	54 (40.6%)	10 (45.5%)	.82
Concomitant procedure	16	13 (9.8%)	3 (13.6%)	.70
Coronary revascularization	8	6 (4.5%)	2 (9.1%)	.32
Other concomitant procedure	8	7 (5.3%)	1 (4.5%)	>.99
Severe pulmonary arterial hypertension	16	12 (9.4%)	4 (23.5%)	.10
Aspirin	117	101 (77.1%)	16 (72.7%)	.79
Clopidogrel	60	55 (42.0%)	5 (22.7%)	.10
Vitamin K antagonist	34	28 (21.4%)	6 (27.3%)	.58
Novel anticoagulants	7	6 (5.6%)	1 (7.7%)	.56
Vitamin K antagonist or novel anticoagulants	41	34 (26.2%)	7 (31.8%)	.61
Body mass index (kg/m^2)	155	27.70 (24.95-30.90)	28.95 (25.30-32.05)	.44
Brain natriuretic peptide (pg/mL)	136	1243. (367-2798)	2005.50 (745-60.26.2)	.17
Baseline ACEF score (%)	153	3.32 (1.46-4.79)	4.36 (3.57-5.81)	<.01
Age (years)	155	80.94 (76.99-84.84)	83.65 (77.33-86.77)	.26
GFR (mL/min/1.73 m^2)	154	45.41 (34.19-66.18)	35.50 (27.62-45.13)	<.01
Creatinine baseline (mg/dL)	154	1.18 (0.97-1.53)	1.64 (1.13-2.08)	<.01
EuroScore II (%)	137	4.24 (2.44-8.42)	5.47 (4.07-10.03)	.12
Society of Thoracic Surgeons score (%)	155	5.31 (3.78-8.49)	7.70 (4.79-9.83)	.10
Hemoglobin (g/L)	101	116.50 (99.25-130.75)	111.00 (100.00-129.50)	.96
Total constrast volume during TAVI (mL)	153	186 (72.60-270.00)	151 (55.00-295.75)	.08
Weight (kg)	155	73.00 (65.50-85.00)	77.50 (69.00-85.25)	.41
Contrast/GFR ratio	152	2.96 (1.48-5.86)	2.14 (1.20-6.56)	.44
Echocardiographic characteristics				
Mitral regurgitation ≥ grade II	29	22 (17.1%)	7 (33.3%)	.13
Tricuspid regurgitation ≥ grade II	17	17 (13.2%)	0 (0.0%)	.13
Mean gradient (mm Hg)	154	40.50 (34.00-53.75)	37.50 (30.75-49.25)	.15
Aortic valve area (cm^2)	145	0.75 (0.60-0.90)	0.80 (0.70-1.00)	.05
Ejection fraction (%)	154	57.00 (40.00-60.00)	54.00 (42.50-65.00)	.76

Data provided as number (%) or median (range).
ACEF = age, creatinine, ejection fraction; AKI = acute kidney injury; GFR = glomerular filtration rate by Cockcroft-Gault equation.

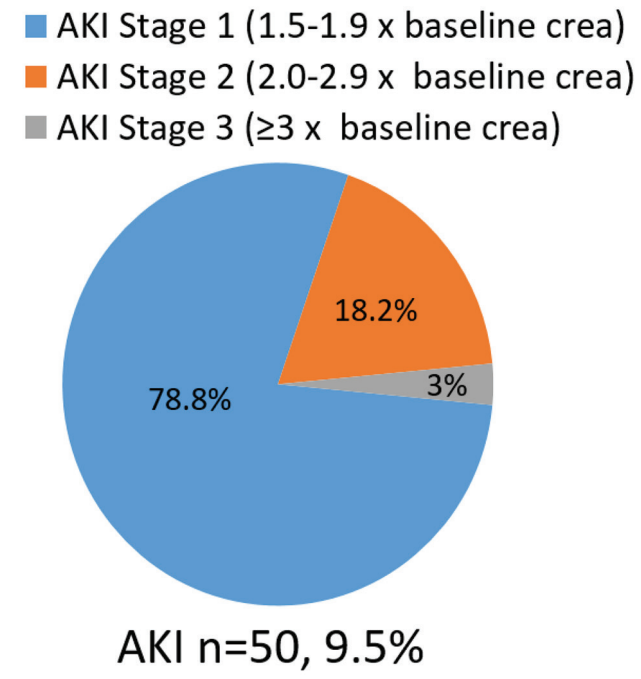

FIGURE 1. Acute kidney injury (AKI) stages: fifty patients (9.5%) of the entire population developed AKI; 78.8% of these patients were stage 3 AKI. crea = creatinine.

a mean contrast volume of 187.3 mL in Yamamoto et al[28] and 261.66 mL in Marbach et al.[31] Madershahian et al[32] discuss the elevated risk of AKI after TAVI in patients with a contrast-agent burden >100 mL, which correlated with the findings of previous studies about percutaneous coronary intervention (PCI).[33,34] However, no unnecessary volume of contrast agent was applied to our cohort. According to our data, operators should pay special attention to the amount of contrast used in DM patients. Whether the RenalGuard System (RenalGuard Solutions) reduces the risk of AKI in this particular patient population requires more data.[35,36]

Although the overall contrast volume used in DM patients who developed AKI was lower than in non-DM patients, a higher ratio of contrast to GFR was documented in DM vs non-DM patients (mean, 5.72 vs 4.32, respectively). From our findings, we are proposing that future prospective studies should evaluate a threshold contrast volume to GFR ratio for DM and non-DM patients. At this point, some publications have established a maximum ratio to predict AKI development post TAVI, which could serve as a guide. Giannini et al[37] suggest that a ratio of >3.2 is correlated with a higher incidence of AKI and mortality after TAVI, whereas Gul et al[38] published a ratio of >3.9 to predict postprocedural contrast induced nephropathy (CIN). For DM patients, Wang et al[39] propose a ratio of >3.1 as a possible valuable predictor of CIN after elective PCI, which might also be an indication for TAVI.

Assessing the ideal combination of ionic/non-ionic and osmolality contrast agents or using dilute contrast agent could lead to fewer incidents of AKI. In the high-risk DM group, the outcome of kidney function could be improved by staging the contrast exposure. For instance, aortography could be performed at earlier dates and co-registered onto operative monitors at the time of TAVI. We further suggest assessment and optimization of nephrotoxic medication prior to TAVI. However, Rosenstock et al[40] found that the incidence of CIN

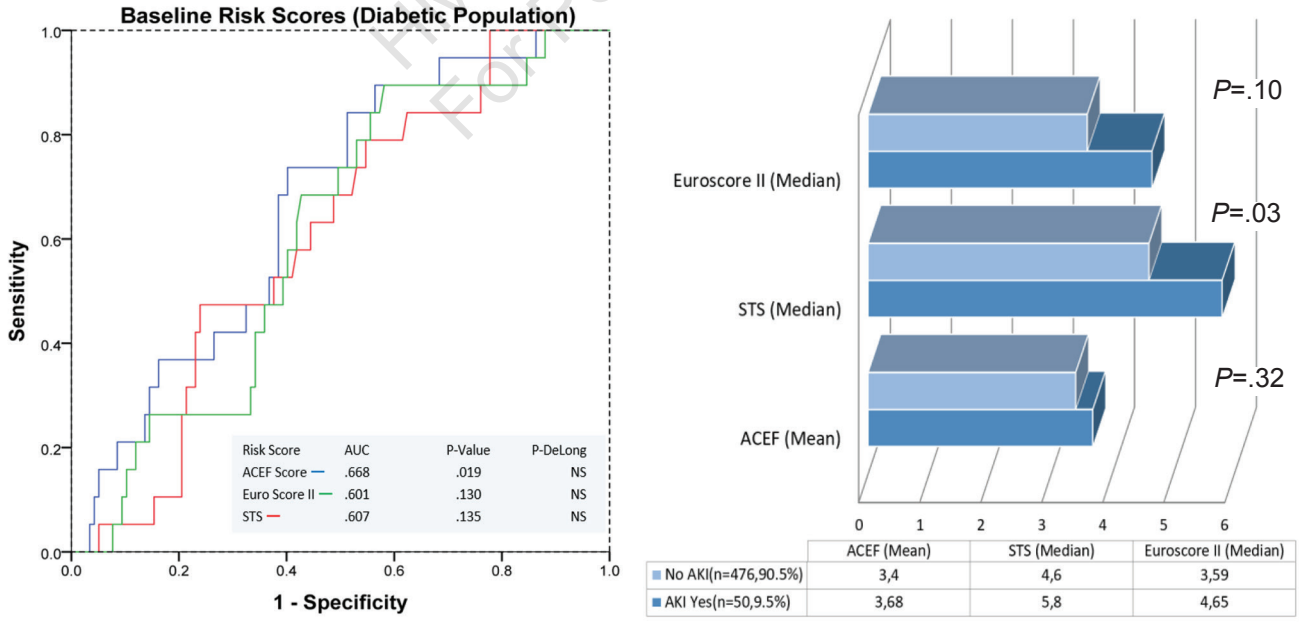

FIGURE 2. Comparison of baseline risk scores in the whole population.

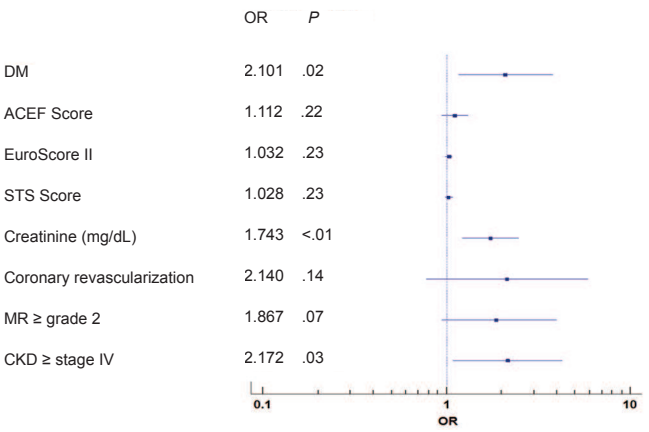

FIGURE 3. Univariate logistic regression model for the whole population.

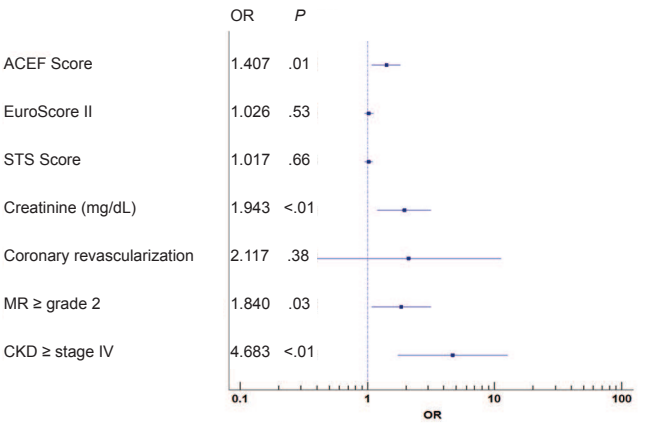

FIGURE 4. Univariate logistic regression model for the diabetics subgroup.

in stable patients with CKD stages III or IV does not seem to be influenced by withholding angiotensin-converting enzyme inhibitors or angiotensin receptor blockers 24 hours before coronary angiography. However, postprocedural hydration should be optimized, and fluid resuscitation guided by left ventricular end-diastolic pressure could be reasonable to lower the risks for both prerenal and intrarenal causes of acute renal failure.[41]

For patients with severe renal impairment, contrast avoidance strategies should be evaluated. Alternative non-contrast based imaging modalities for aortic annulus area measurement, such as transesophageal echocardiogram,[42] three-dimensional transesophageal echocardiogram,[43] or cardiovascular magnetic resonance,[44] could be offered.

Study limitations. Our study has the inherent limitations of any retrospective study. Even though it includes data from two Swiss centers, a country-wide analysis would be more significant. Some risk factors, such as valve calcification and renal arteriosclerosis, were not assessed.

Conclusion

DM is a significant predictor for AKI after TAVI. In this high-risk subgroup, baseline creatinine in combination with amount of contrast agent used over GFR influence postprocedural acute renal failure. Overall poor renal function and a high STS score predict renal failure after TAVI. Special attention should be given to the amount of contrast agent used during interventions.

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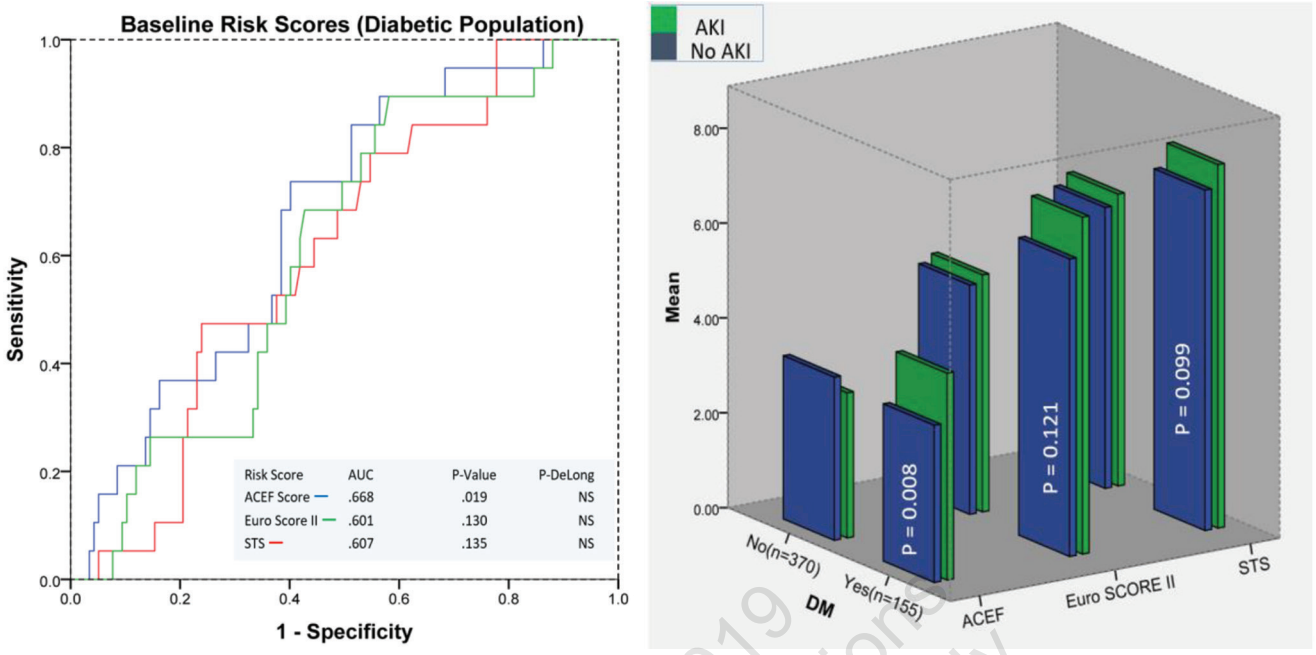
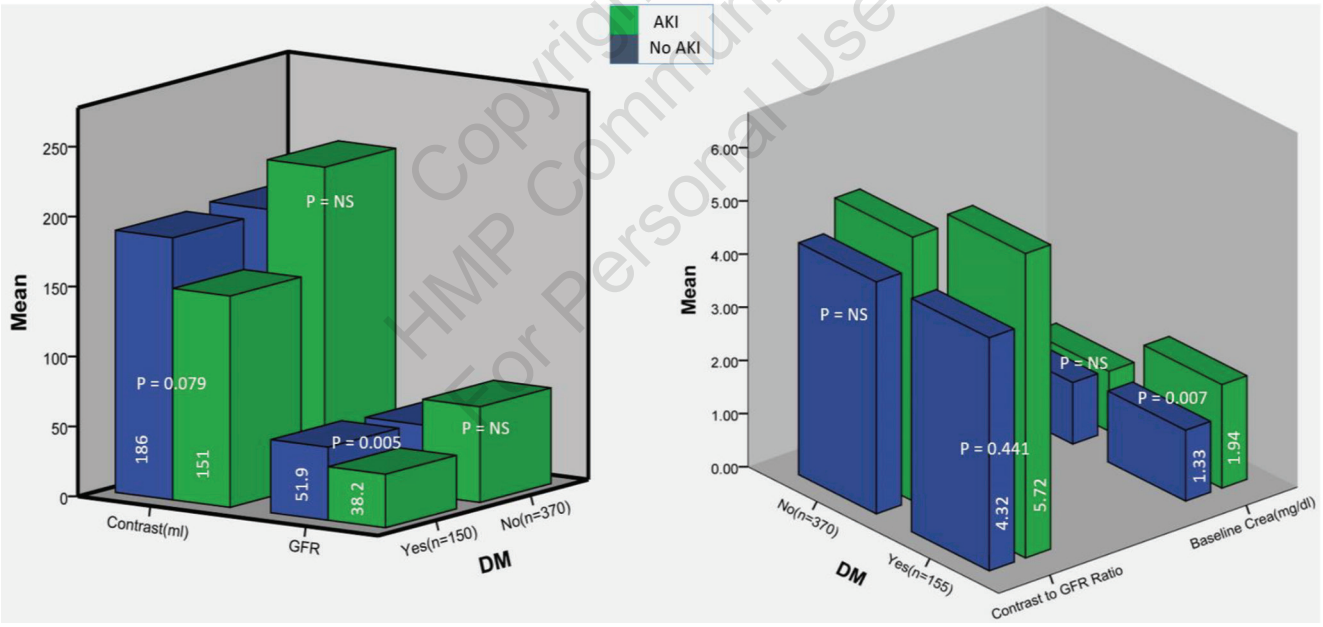


SUPPLEMENTARY FIGURE S1. Comparison of baseline risk scores in the diabetics supgroup.



SUPPLEMENTARY FIGURE S2. Renal parameters and ratio of contrast to glomerular filtration rate.